REMARKS

Claims 1, 3-15 and 17-19 are pending in the current application. Claims 11-15 and 19 are withdrawn. Claim 1 is in independent form. Claims 1, 3, 4 and 11 have been amended. Claims 2 and 16 have been cancelled. In view of the above amendments and following remarks, favorable reconsideration and allowance of the present application is respectfully requested.

Initially, Applicants appreciate the Examiner's indication that the references submitted in the Information Disclosure Statements filed on June 20, 2005 and January 25, 2007 have been considered.

Applicants note that the Examiner has not i) indicated whether the drawings of Figs. 1-10 filed on June 20, 2005 are accepted, or objected, to by the Examiner, and ii) acknowledged that all certified copies pertaining to foreign priority claimed under 35 U.S.C. §119 have been received. As there is no discussion in the *Detailed Action* indicating that the drawings are objected to, or that some or none of the certified copies of the priority documents have been received, Applicants will assume that the drawings of Figs. 1-10 are acceptable and that all certified copies of the priority documents have been received unless indicated otherwise in the next Patent Office communication.

I. CLAIM OBJECTION

Claim 16 stands objected to as being a substantial duplicate of claim 4.

By the present Amendment, Applicants submit that dependent claim 16 has been cancelled. Thus, Applicants submit that the objection has been overcome.

Withdrawal is respectfully requested.

II. EXAMPLE EMBODIMENTS

Example embodiments teach that "[t]he influence of binding events in a monomolecular layer of probe molecules, immobilized on the sensor area or the electrodes, on the electric field or on the impedance of the electrode arrangement is correspondingly low. Due to the fact that, according to an embodiment of the invention, the electrode arrangement is embedded at least partially in a hydrophilic reaction layer containing probe molecules and permeable for target molecules, it is possible to collect within the reaction layer a much higher number of probe molecules or target sequences than in a monomolecular layer. This results in a much larger influence of the electric field or of the impedance-spectroscopic recording range of the electrode arrangement." Specification, paragraphs [0012] and [0013]. Thus, according to example embodiments, probe molecules are attached directly to the micro-spots of the biochips, and dissolved in the reaction layer. As such, more probe molecules are present than with a single layer of probe

molecules attached directly to the electrodes. And, more target molecules can hybridize with probe molecules, and thus be detected.

Other example embodiments teach that "[o]wing to their electric partial charges, the nucleotide sequences held in a microspot by hybridization with immobilized probe molecules alter electrical parameters such as, for example, the conductance within a microspot or the impedance of an electrode arrangement. This makes possible an electrochemical or electrical evaluation using a device of an embodiment of the invention including a biochip with microelectrode arrangement." Specification, paragraph [0010]. Thus, example embodiments teach that hybridization events are detected electro-chemically with the aid of a micro-electrode arrangement.

III. CITED ART GROUNDS OF REJECTION

Claims 1-4, 7, 8, 16 and 17 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Cheng et al. (hereinafter "Cheng"), U.S. Patent Publication No. 2002/0155586; claims 5 and 6 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheng in view of Ghodsian, U.S. Patent Publication No. 2002/0115293; and claims 9, 10 and 18 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheng in view of Strizhkov et al. (hereinafter "Strizhkov"), PCR amplification on a microarray of gel-immobilized oligonucleotides: detection of bacterial toxin- and drug-resistant genes and their mutations, Bio Techniques (2000). Applicants respectfully traverse the rejections.

A. INDEPENDENT CLAIM 1

Amended independent claim 1 is directed to a method for PCR amplification and detection of nucleotide sequences including (*inter alia*) "using a hydrophilic reaction layer having coupling groups for covalent binding of probe molecules and an array of a plurality of microspots forming analytical positions" and "detecting hybridization events on probe molecules immobilized at one analytical position with the aid of a microelectrode arrangement." Applicants submit that the art relied upon in the rejection fails to teach, or suggest, the above features recited in amended independent claim 1.

i. CHENG

The rejection states that "...Cheng teaches a method wherein a hydrophilic reaction layer, such as a [hydrogel] based on acrylamide and having coupling groups for covalent binding of probe molecules is used (paragraph 60, lines 14-21 and paragraph 92, lines 1-10)." Action, p. 4. Applicants respectfully disagree for the following reasons.

Cheng is directed to a standard method for amplification and detection of nucleic acids with the aid of a biochip wherein "...these chips are coated with a thin permeation layer 25 such as a hydrogel, agarose, a polymer of acrylamide, or a sol-gel matrix or the like. This permeation layer 25 protects the cells and molecules of interest (i.e., biomaterials) from the electrochemistry occurring at the electrode surface that would otherwise damage the biomaterials (or the ability to assay them) if they were exposed

directly to the electrodes." Cheng, paragraph [0060]. Thus, the hydrogel in Cheng protects the electrodes, and functions as a type of filter that is permeable to the nucleic acids to be detected.

In addition, Cheng teaches that "[t]he third stage of sample handling comprising detection of the molecules of interest is preferably carried out for proteins and nucleic acids of interest. Such detection can use various forms of hybridization to probes previously attached to the microarray." Cheng, paragraph [0091] (Emphasis Added). Therefore, the probes of Cheng are attached directly to the microarray as a single layer, not dissolved in the hydrogel and attached to the electrodes. Therefore, Applicants submit that Cheng fails to explicitly teach, or otherwise suggest, that the permeation layer 25 has "coupling groups for covalent binding of probe molecules" as recited in amended independent claim 1.

Furthermore, Cheng teaches that "[t]he target nucleic acid is biased against a positive sinusoidal signal generated using a function generator/arbitrary wave form generator (33120A, Hewlett Packard, Santa Clara, Calif.). The capture probe-target hybrids are then detected using fluorophore-labeled reporter probes and the CCD-based optical imaging system employed for the portable instrument shown in FIG. 2." Cheng, paragraph [0092]. Therefore, Cheng teaches optical detection of target nucleic acids wherein the electrodes of the micro-array function only to collect the target nucleic acid at the electrode in order to achieve a better reaction with the probe molecules attached to the electrodes. That is, the electrodes of Cheng are not used for detection. Further, Applicants submit

that Cheng fails to teach, or suggest, using probe molecules dissolved in the permeation layer with the aid of the electrodes for detection.

For at least these reasons, Applicants submit that Cheng fails to teach, or suggest, a method for PCR amplification and detection of nucleotide sequences including "using a hydrophilic reaction layer having coupling groups for covalent binding of probe molecules and an array of a plurality of microspots forming analytical positions" and "detecting hybridization events on probe molecules immobilized at one analytical position with the aid of a microelectrode arrangement" as recited in amended independent claim 1.

ii. SECONDARY REFERENCES: GHODSIAN AND STRIZHKOV

Applicants submit that the secondary references fail to cure the deficiencies of Cheng with respect to amended independent claim 1.

Namely, Ghodsian is directed to an optical sensor configured with silicon technology that can detect DNA fragments. The DNA fragments are obtained using a standard electrophoresis device. Ghodsian fails to teach, or suggest, i) electro-chemical detection with the aid of electrodes that are coated with probe molecules or ii) arranging probe molecules in a gel that is applied over the metal electrode and arranging probe molecules in a single layer on the electrodes.

Strizhkov is directed to a standard method for PCR in a gel pad wherein optically active molecules marked in the gel are subsequently detected with the aid of an optical fluorescence measurement. Strizhkov

fails to teach, or suggest, embedding electrochemical electrodes in a hydrogel wherein the electrodes are coated with probe molecules and probe molecules are dissolved in the gel.

Therefore, Applicants submit that Cheng, individually or in combination with Ghodsian and/or Strizhkov, fails to expressly teach, or otherwise suggest, all the features of amended independent claim 1,

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection to independent claim 1, and claim 3-10, 17 and 18 at least by virtue of their dependency on independent claim 1.

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CONCLUSION

Accordingly, in view of the above, reconsideration of the rejections and allowance of each of claims 1, 3-15 and 17-19 in connection with the present application is earnestly solicited.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) hereby petition(s) for a two (2) month extension of time for filing a reply to the outstanding Office Action and submit the required $460.00 extension fee herewith.

Should there be any matters that need to be resolved in the present application; the Examiner is respectfully requested to contact the undersigned at the telephone number below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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